REMARKS

Statement of Substance of Interview Under 37 C.F.R. § 1.133(b)

In accordance with 37 C.F.R. § 1.133(b) and M.P.E.P. § 713.04, Applicants herein provide a summary of the interview between Applicants' representatives and Examiner Wax conducted on June 21, 2006 ("the interview"). Applicants thank Examiner Wax for agreeing to conduct the interview and appreciate the courtesies extended by the Examiner.

During the interview, Applicants' representatives discussed several novel aspects of the invention with the Examiner. In particular, Applicants were the first to discover that an O-acetylserine byproduct is formed during the culturing of atrial natriuretic peptide (ANP). Applicants addressed the production of O-actylserine in ANP and developed a method for decreasing its production, while improving production of ANP through the addition of at least one of histidine, methionine or glycine. Applicants' representatives explained that the instant claims reflect this new method and claim the step of reducing the occurrence of O-actylserine in ANP by the addition of at least one of histidine, methionine or glycine.

During the interview, Applicants' representatives discussed claims and arguments that would accompany a Request for Continued Examination. During the interview, Examiner Wax indicated such amendments/arguments would likely be viewed favorably and result in the removal of the obviousness rejection over U.S. Patent 5,670,340 ("the '340 patent"). Applicants believe the below amendments/arguments are consistent with the discussion held during the interview. In the event Examiner Wax disagrees, Applicants would appreciate a call to discuss the response further.

Initially, Applicants reiterated that claims 9-11 are novel and non-obvious in view of the '340 patent because the '340 patent fails to teach or suggest the step of adding at least one of histidine, methionine or glycine for reducing the formation of the O-acetylserine byproduct. Applicants have added dependent claims 13 and 14, which recite that the amount of methionine effective to reduce formation of the byproduct is 3 g/L. Applicants have also added dependent claims 15 and 16, which are directed to the addition of methionine and at least one of histidine or glycine. Applicants have further added independent claims 17-20, which relate to reducing the formation of a byproduct polypeptide by adding at least one of histidine or glycine.

Amendments to the Claims

Upon entry of the foregoing amendment, claims 3-6 and 8-20 are pending in the application. Claims 13-20 are newly added.

Applicants respectfully request entry of the above amendment and submit that the above amendment does not constitute new matter. Support for new claims 13-20 can be found throughout the specification and in the claims as originally filed. Support for claims 13 and 14 can be found, for example, in Example 3 of the specification. Support for claims 15 and 16 can be found, for example, at page 9 of the specification. Support for claims 17-19 can be found, for example, at pages 5, 8, 10-12 and Example 3 of the specification. Support for claim 20 can be found, for example, in Example 3 of the specification.

Based on the above amendment and the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding rejections and that they be withdrawn.

Certified Priority Document

The Office Action acknowledges the instant application's claim of priority to JP 2000-137228. *See* O.A. at page 2. However, the Office Action states that the priority documents are not on file and that Applicants are required to submit a copy of the priority documents.

Applicants respectfully submit that a copy of the certified priority document of JP 2000-137228 ("the certified priority document") was previously submitted to the USPTO. A copy of the certified priority document submitted on November 16, 2005 is attached herewith for the Examiner's convenience as **Exhibit A**. A copy of the date-stamped postcard indicating receipt of the certified priority document is attached herewith as **Exhibit B**.

Rejections Under 35 U.S.C. § 103(a)

Claims 3-6 and 8-12 were rejected under 35 U.S.C. § 103(a) as allegedly being obvious over the '340 patent. Applicants respectfully traverse this rejection.

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success.

Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. *See* M.P.E.P. §§ 2142-2143 (8th ed., Rev. No. 3).

The Office Action cites to the '340 patent as teaching the production of human calcitonin and CNP-22 from fusion proteins in E. coli. *See* O.A. at pages 2 and 3. The Office Action states that while the '340 patent does not teach the production of ANP from a fusion protein in E. coli, it would have been obvious to a person of skill in the art to substitute ANP for human calcitonin or CNP per the teachings of the '340 patent because the same result should be expected when using ANP in place of CNP or calcitonin. *See* O.A. at page 3.

Applicants respectfully traverse. Claims 9 and 10 are directed to methods comprising (i) culturing transformed host cells that produce a recombinant atrial natriuretic peptide comprising a serine residue and a byproduct polypeptide comprising an O-acetylserine residue in place of a serine residue; (ii) adding at least one of histidine, methionine or glycine in an amount effective to reduce said byproduct formation; and (iii) reducing the formation of said byproduct polypeptide. Claim 11 is directed to a medium comprising said transformed host cells, at least one of a histidine, methionine or glycine added to the medium and a reduced formation of said byproduct polypeptide as compared with a control medium with no histidine, methionine or glycine added.

Applicants respectfully submit that the '340 patent fails to provide the requisite teaching or motivation to render the claimed invention obvious. As an initial matter, the '340 patent is directed primarily to calcitonin or CNP. As such, it is silent with regard to the production of any byproducts when producing calcitonin or CNP. Indeed, there is no discussion of actually producing ANP or any byproduct that may or may not be present in such a production. As the '340 patent provides no discussion of byproducts, one skilled in the art would not be motivated to alter the teachings of the reference to reach the claimed invention — reducing byproducts formed during ANP production.

Further, the '340 patent fails to disclose or suggest the specific byproduct polypeptide comprising an O-acetylserine residue in place of a serine residue that occurs when producing ANP. Additionally, the '340 patent does not teach or suggest adding at least one of histidine, methionine, or glycine to reduce formation of a byproduct polypeptide of any peptide during the culturing procedure, let alone a byproduct polypeptide comprising an O-acetylserine residue in

place of a serine residue for ANP production. As such, the '340 patent fails to render obvious the claimed invention, at least because it fails to produce ANP according to the claimed invention, fails to provide a discussion of the reduction of any byproduct polypeptide, in particular O-acetylserine, and fails to teach the introduction of at least one of histidine, methionine or glycine to reduce byproduct formation. Accordingly, Applicants respectfully submit that the U.S.P.T.O. has not established a *prima facie* case of obviousness because the '340 patent does not teach or suggest each and every claim limitation.

The Office Action maintains the rejection and states the '340 patent teaches a process for the production of a protein (including atrial natriuretic peptide) comprising culturing E. *coli* host cells transformed. The Office Action further states that broth media used during the incubation or growth step of the host cell in the E. *coli* comprises 2.9 g/L of L-methionine, and thus, the product and method are taught. *See* O.A. at page 4.

Applicants respectfully traverse. As an initial matter, Applicants believe the Office Action contains a typographical error and note that in Example 3 of the '340 patent, the media contained 2.0 g/L of L-methionine, not 2.9 g/L of L-methionine. Applicants also note the addition of dependent claims 13 and 14, which recite that the amount of methionine effective to reduce formation of the byproduct is 3 g/L. Applicants respectfully submit that the '340 patent does not teach or suggest the addition of 3 g/L of methionine.

As discussed above, the '340 patent is silent on the formation of a byproduct and the addition at least one of histidine, methionine or glycine in an amount effective to reduce formation of said byproduct. Applicants further submit that the '340 patent only describes a method of producing proteins, and neither teaches nor suggests a method for, or the step of, reducing the byproduct polypeptide as required by the claims. For example, claim 9 is drawn to a method for reducing formation of a byproduct polypeptide and both claims 9 and 10 require the step of reducing the formation of the byproduct polypeptide.

Applicants also assert that '340 patent does not teach the media of claims 11 and 12. The medium of Claim 11 comprises a reduced formation of the byproduct polypeptide "as compared to a control medium with no histidine, methionine or glycine added." In claim 12, the formation of said byproduct is "reduced in an amount greater than or equal to 50% as compared with said control medium." However, the '340 patent does not teach or suggest a media comprising a

reduced formation of the byproduct polypeptide (e.g., in an amount greater than or equal to 50%) as compared to a control. Accordingly, Applicants maintain that the '340 patent fails to teach each and every claim limitation of the instant claims.

As a general issue, the Office Action states that Applicants' arguments were relying on preambulatory language. For instance, the U.S.P.T.O. purports that claim 9 only requires the step of culturing, and the recitation of "O-acetylserine" is limited to the preamble of the claims or as the inherent end-point of the claimed method. Applicants respectfully submit that the body of the claims contain the limitations that distinguish the claimed invention from the '340 patent as discussed above. For example, claim 9 recites three method steps, each of which contain the recitation of the O-acetylserine byproduct. Step (i) of claim 9 recites, "culturing...transformed host cells that produce...*a byproduct polypeptide comprising an O-acetylserine residue*," step (ii) recites, "an amount effective to reduce *said byproduct* polypeptide" and step (iii) recites, "reducing the formation of *said byproduct polypeptide*." (emphasis added). Accordingly, Applicants respectfully submit that the Office Action improperly limits claim 9.

The Office Action states the byproduct O-acetylserine has no effect on the steps performed in the methods of claims 10-12 and therefore the recitation of "O-acetylserine" does not limit the claims. The U.S.P.T.O. supports this statement by citing to M.P.E.P. § 2105 for the proposition that "language that suggests or makes optional, but does not require steps to be performed or does not limit a claim to a particular structure does not limit the scope of a claim or claim limitation." *See* O.A. at page 5.

Applicants respectfully traverse. Initially, Applicants submit that claims 11-12 are directed to culture media rather than methods. Applicants further assert that claim 10, like claim 9 discussed above, contains the recitation of the O-acetylserine byproduct *in each method step*. Accordingly, Applicants respectfully submit that the Office Action improperly limits claim 10.

Applicants reviewed M.P.E.P. § 2105 and were unable to find the language discussed in the Office Action regarding "language that suggests or makes optional, but does not require steps to be performed or does not limit a claim to a particular structure does not limit the scope of a claim or claim limitation." Applicants respectfully request clarification as to where M.P.E.P. § 2105 specifically relates to the issues raised by the Examiner should the rejection not be removed.

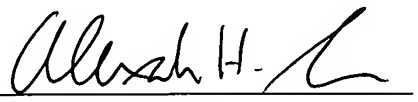
For the foregoing reasons, Applicants respectfully request the Examiner to withdraw all of the 103(a) rejections over the '340 patent.

CONCLUSION

Applicants respectfully request consideration of the above remarks. In view of the above remarks, early notification of a favorable consideration is respectfully requested.

Respectfully submitted,

Dated: September 13, 2006

By: 

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